REMARKS

Claims 1-9 and 11-13 remain in the application. Only Claim 1 is in independent form.

Applicants wish to thank Examiner Desai for the courtesies extended to applicants' representatives Mr. David Kurlandsky and Ms. Emma Dolan during a November 14, 2003 telephone interview. During this telephone conference, the Gilligan et al. and Gyermek references were discussed. The Examiner indicated that she would revisit these references in light of the telephone interview.

The outstanding Office Action sets forth a final rejection of Claims 1-9 and 11-13 under 35 U.S.C. §103 over Gilligan et al. and Gyermek.

It is stated in the outstanding Office Action that the prior art teaches similar compounds to treat migraine and pain which allegedly render the claimed invention obvious over the prior art.

As stated in our previous response, Gilligan discloses tetralin compounds similar to those of the present invention which are stated to have good affinity for the 5-HT_2 receptor and which are related to DuP734, a known 5-HT_2 antagonist.

With regard to Gyermek, applicants respectfully submit that when the full text (a copy provided herewith) of Gyermek is reviewed rather than the abstract, that the presently claimed invention is readily distinguishable from the teachings of Gyermek. As was stated in the previous Office Action and as is maintained in the outstanding Office Action, it is argued that "Laszlo Gyermek clearly teaches that serotonin is widely distributed in the body within the central and peripheral nervous systems. It also teaches that serotonin inhibitors can also treat pain syndromes (see page 402 of the reference)." This quotation is referring to the last sentence of paragraph 2 of page 402, which states "Future use of these drugs is also envisioned in the treatment of certain types of pain syndromes." This statement is ambiguous, as it is not clear to which drugs it refers, and it should therefore be interpreted in light of the full text of

the Gyermek reference. Applicants assert that this sentence has been interpreted to refer to all drugs mentioned in the paragraph and, thus, to mean 'Future use of [serotonin receptor subtype agonists and antagonists and serotonin reuptake inhibitors] is envisioned in the treatment of certain types of pain syndromes.' Applicants previously submitted and reiterate herein that the term "these drugs" refers only to the "serotonin reuptake inhibitors discussed in the preceding sentence.

The interpretation set forth in the Office Action is clearly contradicted by the full text of the Gyermek article, in particular by the discussion on pages 417-418 of analgesia and the role of various serotonin receptor subtypes. Although on page 417 (last paragraph) there is a very general statement that "the serotonin receptors that may participate in central pain procession are 5-HT_1, 5-HT_2, 5-HT_3, and 5-HT_4 subtypes" (emphasis added), it is also stated that "The degree of participation of different serotonin receptors in nociception and analgesia is variable." The only specific discussion of the 5-HT_2 receptor subtype in this context is on page 418 (first paragraph), where it is stated that "5-HT_2 agonists, acting on the brain stem could provide new types of analgesics" (emphasis added). There is no teaching nor suggestion that 5-HT_2 antagonists could be be useful in the treatment of pain syndromes. Gyermek provides no motivation to the skilled person to investigate 5-HT_2 antagonists in the treatment of pain.

There is a very general and speculative statement on page 407 of Gyermek that "Other possible applications of 5-HT_2 receptor blocking drugs include symptomatic treatment of migraine..." However, the only 5-HT_2 receptor blocking drug discussed in this context is Ketanserin, a selective 5-HT_{2A} antagonist which is known to be inactive as a migraine treatment (Kalkman and Fozard- see Applicants' May 19, 2003, response). The speculative statement on page 407 of Gyermek, therefore, does not provide motivation to the skilled person, possessing the knowledge that Ketanserin is not useful for the treatment of migraine, to investigate 5-HT_2 receptor blocking drugs for the treatment of migraine or other pain syndromes.

The Gilligan et al. article teaches that the compounds of the present invention are 5-HT_2 antagonists and Gyermek teaches that 5-HT_2 agonists may be useful for the treatment of pain. 5-HT_2 antagonists prevent 5-HT binding to the receptor while agonists activate the receptor. Gyermek therefore provides no motivation for the skilled person to compounds such as those disclosed in Gilligan, which are known to be 5-HT_2 antagonists, for the treatment of pain syndromes. Thus, the present is therefore not rendered obvious by the combination of Gilligan and Gyermek.

In view of the foregoing remarks, reconsideration of the rejection and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any over payment in connection with this communication to our Deposit Account No. 23-0455.

Respectfully submitted,

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David R. Kurlandsky
Registration No. 41,505
Warner-Lambert Company
2800 Plymouth Road
Ann Arbor, MI 48105
Telephone: (734) 622-7304
Facsimile: (734) 622-1553